REMARKS

In the Final Action dated April 20, 2004, claims 1-17, 23 and 27-29 are pending and under consideration. Claims 1, 4-17, 23 and 27-29 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the written description requirement.

This Response addresses the Examiner's rejection. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

The Examiner has rejected claims 1, 4-17, 23 and 27-29 under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the written description requirement. The Examiner states that the reasons for the rejection are set forth in the previous office action, mailed July 29, 2003. In the previous Office Action, the Examiner alleged that the vectors described in the specification are limited to those containing the zeocin resistance gene. The Examiner also alleged that there is no structure-function analysis in the specification of the disclosed zeomycin resistance conferring protein, which would provide guidance on the selection of other resistance marker genes that may function in both insect and prokaryotic cells.

In response, Applicants respectfully submit that the claimed shuttle vectors are characterized by a selectable marker coding sequence, which is linked to a promoter region comprising an insect cell promoter and a prokaryotic promoter. The selectable marker is expressed in insect cells and bacterial cells that are transformed with the shuttle vector, and confers a phenotype selectable in both insect cells and bacterial cells. The vectors of the present invention have the advantage of utilizing one selection marker that is effective for selection in both insect cells and prokaryotic cells. A shuttle vector containing a selectable

marker, which confers resistance to a bleomycin/phleomycin-type of antibiotic, is merely a preferred embodiment of the present application.

Applicants previously asserted that the specification describes that the shuttle vectors of the present invention can be adapted for use with a variety of antibiotic selection schemes other than zeocin selection, as stated in the specification on page 67, lines 20-21, for example. The Examiner nevertheless maintains in the Final Action that the specification does not describe other resistance marker genes encoding proteins that function in both insect cells and prokaryotic cells. In addition, the Examiner refers to the statements on pages 25 and 27 of the specification, which the Examiner has interpreted as an indication of unpredictability of the use of selection markers.

Applicants believe that the Examiner is referring to the following paragraphs in the specification.

> As noted previously, many known selection systems exhibit the undesirable characteristic that transforming DNA sequences are amplified over time in the presence of antibiotic selection. These amplified DNA sequences may be unstable and are liable to be rapidly lost in the absence of continued selection. This section discloses experiments that evidence the stability of transforming sequences in insect cell lines transformed to Zeocin resistance in accordance with the present invention.

See, page 25, lines 22-27.

> The results show an unexpected advantage of the present invention, ie. stability of transforming DNA sequences. The stability of transforming DNA sequences in cell lines of the invention contrasts with the prior art reports discussed above which disclose the frequency with which amplification, and attendant genomic instability, may occur when using prior art selection system.

See, page 27, lines 3-7.

It is clear from these paragraphs that the undesirable characteristic of amplification

and instability of transforming DNA is associated with "known" selection systems, i.e., selection systems in the prior art. The presently claimed vector, characterized by having one marker in a single vector that is expressed and selectable in both insect cells and prokaryotic cells, is not associated with amplification and instability of transforming DNA. The superior features of the claimed vector, are exemplified by, but by no means limited to, a vector having a zeocin resistance gene. Applicants respectfully submit that the Examiner has misinterpreted the text on page 25 by stating that only zeocin selection avoids the undesired effects.

Applicants reassert that the specification clearly describes that the shuttle vectors of the present invention can be adapted for use with a variety of antibiotic selection schemes other than selection based on a bleomycin/phleomycin-type antibiotic. See page 67, lines 20-21, for example. The specification also illustrates how to make a shuttle vector containing a selectable marker suitable for selection in both insect cells and prokaryotic cells (see e.g., pages 23 and 27). Based on the present teaching, those skilled in the art would understand that Applicants had possession of the shuttle vectors as presently claimed at the time of filing of the present application. The written description requirement does not require exemplification of each and every embodiment claimed.

As evidence that the shuttle vector can be adapted with other selection systems, Applicants provide herewith a Declaration of Dr. Grigliatti. As discussed in the Declaration, shuttle vectors are presented which comprise a sequence coding for a marker selectable in both insect cells and prokaryotic cells, wherein the marker confers resistance to phleomycin, hygromycin, puromycin or blastacidin. All the shuttle vectors contain a promoter region comprising an insect promoter and a prokaryotic promoter, which region is operably linked to the selectable marker gene, as characterized in claim 1.

Specifically, vector p2Zop2F (Exhibit B attached to the Declaration), which is the described in the specification (Figure 8a), contains the Opie2 insect promoter and the EM7 prokaryotic promoter, as well as the zeocin resistance gene (Zeo R). As discussed in Paragraph 7 of the Declaration, the vector is also selectable based on resistance to phleomycin in both insect cells and bacterial cells.

Vector p2Hf (Exhibit C attached to the Declaration), contains the Opie2 insect promoter and the EM7 prokaryotic promoter, as well as the hygromycin resistance gene. As discussed in Paragraph 8 of the Declaration, the vector is selectable based on resistance to hygromycin in both insect cells and bacterial cells.

Vector p2PaOp2F+EM7 (Exhibit D attached to the Declaration), contains the Opie2 insect promoter and the EM7 prokaryotic promoter, as well as the puromycin resistance gene (PAC). As discussed in Paragraph 9 of the Declaration, the vector is selectable based on resistance to puromycin in both insect cells and bacterial cells.

Vector p2Ba2F (Exhibit E attached to the Declaration), contains the Opie2 insect promoter and the EM7 prokaryotic promoter, as well as the blastacidin S resistance gene (Blast R). As discussed in Paragraph 10 of the Declaration, the vector is selectable based on resistance to blastacidin S in both insect cells and bacterial cells.

Vectors p2Z2f-EM7, p2PaOp2F, and p2Ba2F-EM7 (Exhibits F-H attached to the Declaration) are essentially the same as p2Zop2f, p2PaOp2F+EM7, and p2Ba2F, respectively, except that the EM7 promoter has been removed. See Paragraphs 11-14 of the Declaration. The Opie2 promoter is active in both insect cells and prokaryotic cells sufficient to drive the expression of the selectable marker gene in both cells. The activity of the Opie2 promoter in prokaryotic cells is described in the specification, e.g., at page 9, lines 22-23, and page 62, line

23 to page 63, line 2. Applicants have added claim 30 to further delineate this embodiment of the present invention.

Applicants respectfully submit that Dr. Grigliatti's Declaration provides evidentiary support for the assertion in the specification that the claimed shuttle vector can be adapted with selection systems other than zeocin. Notably, phleomycin, hygromycin and puromycin are all markers known to those skilled in the art at the time the present application was filed.

In view of the foregoing, it is respectfully submitted that the claimed shuttle vectors are adequately described in the specification in compliance with the written description requirement of 35 U.S.C. §112, first paragraph. Withdrawal of the rejection is therefore respectfully requested.

Claims 31-33 are added to delineate the Opie2 insect promoter elements uniquely identified by the present invention. Support for these claims are found in claims 27-29 and in the specification, e.g., page 9, lines 6-10. No new matter is introduced.

It is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

Frank S. DiGiglio
Registration No. 31,346

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, New York 11530
(516) 742-4343

XZ:ab

Enc.: Declaration with attached Exhibits A-H.